The Examiner argues that Groups I-IV do not relate to a single inventive concept because they lack the same or corresponding special technical feature under PCT Rule 13.2. In support, the Examiner states that the special technical feature is an RNA encoding an antigen in combination with one of a cytokine, a cytokine mRNA, and adjuvo-viral mRNA, a CpG and an adjuvant RNA, and that the technical feature is known in the art, citing Schirmacher *et al.* (hereinafter "Schirmacher"). Applicants respectfully disagree with the Examiner's conclusion.

First, as stated in the specification and repeated in the claims, the general inventive concept of the present invention relates to an mRNA (not any RNA) encoding an antigen and the use thereof in combination with one of a cytokine, a cytokine mRNA, and adjuvo-viral mRNA, a CpG and an adjuvant RNA. See Specification at page 1, paragraph 1, and claim 1. Applicants respectfully submit that the cited reference does not teach the concept of using an mRNA encoding an antigen as claimed in the present application.

Schirmacher discloses an anti-tumor vaccination using a self-replicating infectious RNA encoding a model tumor antigen, wherein Semliki Forest virus replicase drives RNA expression of the lacZ gene coding for β-galactosidase as model tumor-associated antigen (TAA). See Schirmacher, Abstract. Schirmacher further discloses coinjection of cytokine RNA with the disclosed self-replicating RNA. See Abstract and page 1138, left Col., 1st paragraph. As discussed in the present specification at page 4, 2nd paragraph, the most important distinction between Schirmacher and the present application is the use of a self-replicating RNA by Schirmacher. Such a self-replicating RNA *per se* comprises all elements necessary for replication of the RNA including enhancer and promoter sequences and all further regulatory elements.

An mRNA means the RNA transcript of a protein-encoding gene. It does not contain elements necessary for replication of the RNA such as enhancer and promoter sequences but only the coding sequence of an encoded protein. An mRNA does not need Semliki Forest virus replicase for RNA expression since the mRNA may be translated directly by the ribosomes of the organism into the encoded protein. The self-replicating infectious RNA disclosed in Schirmacher necessarily requires Semliki Forest virus replicase for RNA expression of the lacZ gene coding for β-galactosidase as model tumor-associated antigen. See Schirmacher, Abstract.

Accordingly, it is clear that the RNA and the method for immunostimulation disclosed in Schirmacher are different from that disclosed in the present application and does not defeat novelty. Therefore, the Patent Office has not established the presence of the special technical feature of Applicants' claims in the prior art. Accordingly, unity is present, and Applicants respectfully request that the Examiner reconsider the restriction requirement and examine all the claims in one application.

Additionally, Applicants believe that there is no undue burden on the Examiner to search and examine all Groups together. As stated in § 803 of the M.P.E.P. "[i]f the search and examination of the entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." (M.P.E.P. § 803, emphasis added). Because the same art relevant to a method for immunostimulation comprising using an mRNA encoding an antigen of a tumor (Group II) would be also relevant to a similar method using an mRNA encoding an antigen of a pathogen (Group I) and the mRNA used for such method (Groups III and IV), there would be no undue burden on the Examiner to search and examine these Groups together. Accordingly, Applicants respectfully submit that the restriction requirement should be withdrawn even under restriction practice.

Alternatively, Applicants respectfully request that at least Groups II and IV be considered together. Pursuant to 37 CFR § 1.475(b)(3), unity of invention is fulfilled between these two Groups because the claims of Groups II and IV are directed to a product (i.e. Group IV) and a process of use said product (i.e. Group II), which are an acceptable combination of categories for unity. Accordingly, Applicants respectfully request that the Examiner reconsider the restriction requirement and examine at least the claims of Groups II and IV in one application.

The International Examiner Found Unity of Invention

Furthermore, unity of invention was found during the international stage. As shown in the International Preliminary Report on Patentability and International Search Report, all claims were searched and examined together. Thus, application of PCT Rules 13.1 and 13.2 by the International Examiners shows that unity exists. Since the search has already been conducted by the International Search Authority and the International Examination Authority and no lack of

unity of invention has been found, for this additional reason, there would be no undue burden on the Examiner to examine both Groups in one application.

Restriction to a Single Species Is Improper

The Examiner further requires election of species of the genus of tumor antigens as recited in claim 5. Applicants provisionally elect the tumor antigen NY-ESO-1 for further prosecution with traverse for essentially the same reason as discussed above as well as the following reasons.

In making the election requirement, the Examiner refers to PCT Rules 13.1 and 13.2, and alleges that the species recited in claim 5 lack a common structure element. Applicants note, however, that, according to PCT Rule 13.2, the requirement of unity of invention referred to in PCT Rule 13.1 shall be fulfilled when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The term "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. In the present case, the technical relationship, and thus the same or corresponding special technical feature, is the tumor antigen combined into the inventive combination, regardless of the type of tumor antigen. In this case, a common structure element between the mRNA encoding the tumor antigen as a common technical feature is not required. Reconsideration and withdrawal of the requirement to elect a single species is therefore respectfully requested.

CONCLUSION

For at least the above reasons, Applicants respectfully request that the restriction requirement be reconsidered and withdrawn.

Applicants reserve all rights to pursue the non-elected groups and species in one or more divisional application.

Accompanying this response is a petition for a one-month extension of time to and including June 6, 2009 with the required fee payment. No further fee is believed due. However,

if an additional fee is due, the Director is authorized to charge our Deposit Account No. 03-2775, under Order No. 22122-00006-US1 from which the undersigned is authorized to draw.

Dated: June 5, 2009

Respectfully submitted,

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